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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/735,910	12/16/2003	Ru Chih C. Huang	2240-199065	3871

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EXAMINER	
ROYDS, LESLIE A	

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1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/735,910	HUANG ET AL.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9,10,15,18-20 and 22-33* is/are pending in the application.

4a) Of the above claim(s) *22-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-10,15,18-20,32 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 9-10, 15, 18-20 and 22-33 are presented for examination.

Applicant's Amendment filed December 21, 2007 has been received and entered into the present application.

Claims 9-10, 15, 18-20 and 22-33 remain pending. Claims 9-10, 15, 18-20 and 32-33 remain under examination and claims 22-31 remain withdrawn from consideration pursuant to 37 C.F.R. 1.142(b). Claim 9 is amended.

Applicant's amendments and arguments, filed December 21, 2007, have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9-10, 15 and 18-20 remain rejected under 35 U.S.C. 102(b) as being anticipated by Howell et al. (U.S. Patent No. 5,541,232; 1996), already of record, for the reasons of record set forth at pages 2-3 of the previous Office Action dated August 22, 2007, of which said reasons are herein incorporated by reference.

Newly amended claim 9 remains properly rejected in the present case because Applicant's elected compound under examination is the species of M4N (tetra-O-methylnordihydroguaiaretic acid; also known as meso-1,4-bis(3,4-dimethoxyphenyl-(2*R*,3*S*)-dimethylbutane, see Figure 1 of the drawings).

Please see the reply filed August 21, 2006. Such a compound corresponds to Applicant's claimed generic formula wherein R1-R4 are each -OCH3 as evidenced by Figure 1 of the drawings and is still met by the teachings of Howell et al., who teaches the administration of NDGA (*meso*-1,4-bis(3,4-dihydroxyphenyl-2,3-dimethylbutane; col.4, l.33-34) or an analogue thereof (abstract and col.5, l.22-41), such as, e.g., the meso isomer of 1,4-bis(3,4-dimethoxyphenyl)-2,3-dimethylbutane (col.6, l.3-7 and col.16, l.18-col.17, l.9), which corresponds directly to the chemical compound instantly claimed. Please also reference Howell et al. at col.6, l.3-17, where the reference further discloses all stereoisomeric configurations of the disclosed compound 1,4-bis(3,4-dimethoxyphenyl)-dimethylbutane, which anticipates the presently claimed limitation of the (2R,3S) configuration of the elected species.

Response to Applicant's Arguments

Applicant traverses the instant rejection, stating that Howell et al. is directed to the use of catecholic butanes, such as nordihydroguaiaretic acid, for the treatment of multi-drug resistance, which differs from Applicant's claimed use in that Howell et al. inherently requires administration of additional drugs to which the multi-drug resistance develops. Applicant further submits that the generic formula of Howell et al. encompasses thousands of possible drug candidates and asserts that the examples of Howell et al. are limited to NDGA and fail to provide any evidence for any other compounds other than NDGA. Applicant alleges that Howell et al. fails to enable the use of the claimed derivative compounds, wherein R1-R4 are identical and are methoxy or substituted or unsubstituted amino acid residues or salts thereof, for the treatment of leukemia.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

Firstly, the allegation that the instant claims distinguish over the disclosure of Howell et al. because Howell et al. inherently requires administration of additional drugs to which the multi-drug resistance develops is not persuasive. Applicant is attempting to argue patentable distinction over

features that are not claimed. Specifically, Applicant's claims as presently written fail to exclude the concomitant administration of additional drugs to which the multi-drug resistance develops because (1) the claims fail to exclude the use of additional chemotherapeutic agents with, either simultaneously or, more importantly, prior to, the required administration of meso-1,4-bis(3,4-dimethoxyphenyl-(2*R*,3*S*)-dimethylbutane to the claimed subject and (2) present claim 9 contains the transitional phrase "comprising", which is open transitional language and does not patentably exclude the presence or administration of additional components, such as the additional chemotherapeutic agents that cause the multi-drug resistance, to the presently claimed subject (see MPEP §2111.03[R-3] regarding the interpretation of claim transitional language). Moreover, though the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. Please see *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Further, Applicant appears to be of the persuasion that, because Howell et al. discloses a generic structural formula that encompasses a breadth of compounds, the reference to Howell et al. fails to describe the particular of species of compound as instantly claimed with sufficient specificity so as to provide an anticipatory teaching. This is not persuasive. Howell et al. explicitly names the compound in a specific subset of exemplary catecholic butane compounds of the broader generic formula disclosed by the reference. Please see Howell et al., col.6, l.3-7 and col.16, l.18-col.17, l.9. Such an exemplary subset of compounds is clear disclosure and/or suggestion to direct one of ordinary skill in the art to the claimed compound, despite the numerous combinations of substituents taught by the broader disclosure of the reference as a whole, because out of these numerous combinations of substituents, Howell et al. teaches this much smaller, more limited, finite and exemplary set of compounds of the larger generic structure, which anticipates Applicant's presently claimed species.

Moreover, Applicant advances the argument that, because the examples of Howell et al. are directed to the use of the compound NDGA and not the claimed set of compounds (i.e., wherein R1-R4

are each identical and are -OCH3), the reference fails to enable the use of NDGA derivatives for the disclosed cancers, which include, *inter alia*, childhood leukemia, or acute or chronic leukemia (col.6, l.35-40 and col.16, l.18-col.17, l.9). However, the fact that Howell et al. provides exemplary embodiments of the invention using the compound NDGA does not render the reference non-enabled because it fails to present a working or prophetic example of the administration of an NDGA derivative (such as meso-1,4-bis(3,4-dimethoxyphenyl-(2*R*,3*S*)-dimethylbutane) to a leukemic cell and/or a patient suffering from leukemia. The enablement of a disclosure does not hinge on the presence of working or prophetic examples of an embodiment that is very clearly taught and, thus, contemplated by the reference. Please reference MPEP §2164.02, which states, "Compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed…The specification need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970)."

It is, therefore, erroneous and contradictory to the teachings of the MPEP for Applicant to completely discount the disclosure of Howell et al. solely on the grounds that the reference has not provided a working example of the disclosed method(s). Furthermore, Applicant provides no evidence and/or advances no specific reasons (aside from a lack of working embodiments) in support of the conclusion that the reference is not enabled, and, therefore, is alleging non-enablement in the absence of factual support. Please reference MPEP §716.01(c)[R-2](II), which states, "The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, *inoperability of the prior art*, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the

applicant." (emphasis added) In other words, it is insufficient to rely solely on Applicant's opinion of the reference without addressing the totality of evidence in the reference or in the record as a whole, which, in the instant case, clearly provides an anticipatory teaching of the instantly claimed method(s) for the reasons *supra*.

For these reasons, and those previously made of record at pages 2-3 of the Office Action dated August 22, 2007, rejection of claims 9-10, 15 and 18-20 remains proper and is **maintained**.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9-10, 15, 18-20 and 32-33 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Howell et al. (U.S. Patent No. 5,541,232; 1996), already of record, for the reasons of record set forth at pages 3-6 of the previous Office Action dated August 22, 2007, of which said reasons are herein incorporated by reference.

Newly amended claim 9 remains properly rejected in the present case because Applicant's elected compound under examination is the species of M4N (tetra-O-methylnordihydroguaiaretic acid; also known as meso-1,4-bis(3,4-dimethoxyphenyl-(2*R*,3*S*)-dimethylbutane, see Figure 1 of the drawings). Please see the reply filed August 21, 2006. Such a compound corresponds to Applicant's claimed generic formula wherein R1-R4 are each -OCH3 as evidenced by Figure 1 of the drawings and is still met by the teachings of Howell et al., who teaches the administration of NDGA (*meso*-1,4-bis(3,4-dihydroxyphenyl-2,3-dimethylbutane; col.4, l.33-34) or an analogue thereof (abstract and col.5, l.22-41), such as, e.g., the meso isomer of 1,4-bis(3,4-dimethoxyphenyl)-2,3-dimethylbutane (col.6, l.3-7 and col.16, l.18-col.17, l.9), which corresponds directly to the chemical compound instantly claimed. Please also reference Howell et al. at col.6, l.3-17, where the reference further discloses all stereoisomeric configurations of the disclosed compound 1,4-bis(3,4-dimethoxyphenyl)-dimethylbutane, which anticipates the presently claimed limitation of the (2R,3S) configuration of the elected species.

Response to Applicant's Arguments

Applicant traverses the instant rejection, stating that, for the same reasons described above under the rejection set forth under 35 U.S.C. 102(b), the selection of the particular compounds wherein R1-R4 are identical and are –OCH3 or substituted or unsubstituted amino acid residues or salts thereof, for the treatment of leukemia is neither anticipated nor obvious. Applicant alleges there is no reason or even a hint to direct the artisan to select the recited compounds for the treatment of leukemia as instantly claimed.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

Applicant again appears to be of the persuasion that, because Howell et al. discloses a generic structural formula that encompasses a breadth of compounds, the reference to Howell et al. fails to describe the particular of species of compound as instantly claimed with sufficient specificity so as to

provide an adequate teaching to support the *prima facie* obviousness of the claimed subject matter. This is not persuasive. Howell et al. explicitly names the compound in a specific subset of exemplary catecholic butane compounds of the broader generic formula disclosed by the reference. Please see Howell et al., col.6, l.3-7 and col.16, l.18-col.17, l.9. Such an exemplary subset of compounds is clear disclosure and/or suggestion to direct one of ordinary skill in the art to the claimed compound, despite the numerous combinations of substituents taught by the broader disclosure of the reference as a whole, because out of these numerous combinations of substituents, Howell et al. teaches this much smaller, more limited, finite and exemplary set of compounds of the larger generic structure, which clearly renders Applicant's presently claimed species obvious.

Furthermore, Applicant advances the argument that, because the examples of Howell et al. are directed to the use of the compound NDGA and not the claimed set of compounds (i.e., wherein R1-R4 are each identical and are -OCH3), the reference fails to enable the use of NDGA derivatives for the disclosed cancers, which include, *inter alia*, childhood leukemia, or acute or chronic leukemia (col.6, l.35-40 and col.16, l.18-col.17, l.9). However, the fact that Howell et al. provides exemplary embodiments of the invention using the compound NDGA does not render the reference non-enabled because it fails to present a working or prophetic example of the administration of an NDGA derivative (such as meso-1,4-bis(3,4-dimethoxyphenyl-(2*R*,3*S*)-dimethylbutane) to a leukemic cell and/or a patient suffering from leukemia. The enablement of a disclosure does not hinge on the presence of working or prophetic examples of an embodiment that is very clearly taught and, thus, contemplated by the reference. Please reference MPEP §2164.02, which states, "Compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed…The specification need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970)."

It is, therefore, erroneous and contradictory to the teachings of the MPEP for Applicant to completely discount the disclosure of Howell et al. solely on the grounds that the reference has not provided a working example of the disclosed method(s). Furthermore, Applicant provides no evidence and/or advances no specific reasons (aside from a lack of working embodiments) in support of the conclusion that the reference is not enabled, and, therefore, is alleging non-enablement in the absence of factual support. Please reference MPEP §716.01(c)[R-2](II), which states, "The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, *inoperability of the prior art*, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant." (emphasis added) In other words, it is insufficient to rely solely on Applicant's opinion of the reference without addressing the totality of evidence in the reference or in the record as a whole, which, in the instant case, clearly provides teachings that render the instantly claimed method(s) *prima facie* obvious for the reasons set forth *supra*.

Moreover, Howell et al. discloses the generic formula of NDGA compounds, of which the instantly claimed compound meso-1,4-bis(3,4-dimethoxyphenyl-(2*R*,3*S*)-dimethylbutane is explicitly named as an exemplary compound (Howell et al., col.6, l.3-7 and col.16, l.18-col.17, l.9) as effective therapies to treat both solid malignant tumors and hematological malignancies, of which childhood leukemia, acute or chronic leukemia are each specifically named (Howell et al., col.6, l.35-40 and col.16, l.18-col.17, l.9). Contrary to Applicant's allegation, such disclosure provides a clear teaching to guide the skilled artisan to use the compound meso-1,4-bis(3,4-dimethoxyphenyl-(2*R*,3*S*)-dimethylbutane for the treatment of leukemia (i.e., childhood, acute or chronic) and, accordingly, Applicant's argument that the reference fails to provide a hint and/or reason to do so are not found persuasive in this regard.

For these reasons, and those previously made of record at pages 3-6 of the previous Office Action dated August 22, 2007, rejection of claims 9-10, 15, 18-20 and 32-33 remains proper and is **maintained**.

Double Patenting

Obviousness-Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 9-10, 15, 18-20 and 32-33 remain provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 21, 24-26, 30-32, 35, 39-50, 54-62 and 64-72 of U.S. Patent Application No. 11/284,111, already of record, for the reasons of record set forth at pages 6-8 of the previous Office Action dated August 22, 2007, of which said reasons are herein incorporated by reference.

Applicant requests to defer filing a Terminal Disclaimer until allowable subject matter has been indicated.

In view of the fact that allowable subject matter has not yet been identified in the instant case, and further in view of the fact that Applicant has failed to file a Terminal Disclaimer over the cited copending application(s) and also that Applicant has failed to present any arguments or remarks directed to the propriety of the rejection set forth *supra*, the provisional rejection made under the judicially created doctrine of obviousness-type double patenting remains proper and is **maintained**.

Conclusion

Rejection of claims 9-10, 15, 18-20 and 32-33 remains proper and is **maintained**.

Claims 22-31 remain **withdrawn** from consideration pursuant to 37 C.F.R. 1.142(b).

No claims of the present application are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leslie A. Royds/
Patent Examiner, Art Unit 1614

March 19, 2008

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614